INFORMED CONSENT FORM

Official title: Pharmacological Therapy for Calcium Phosphate Urolithiasis

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The University of Texas Southwestern Medical Center at Dallas
Parkland Health & Hospital System

CONSENT TO PARTICIPATE IN RESEARCH

Title of Research: Pharmacological Therapy for Calcium Phosphate Urolithiasis – Aim 1

Funding Agency/Sponsor: UT Southwestern Medical Center – Center for Mineral Metabolism

Investigators:	Telephone No. (regular office hours)	Telephone No. (other times)
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Instructions:
Please read this consent form carefully and take your time making a decision about whether to participate. As the researchers discuss this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. The purpose of the study, risks, inconveniences, discomforts, and other important information about the study are listed below. If you decide to participate, you will be given a copy of this form to keep.

Why is this study being done?
This study is being done to evaluate whether the two medications, citric acid and potassium citrate, can reduce the risk of recurrent kidney stones in people who form calcium phosphate stones.

Why is this considered research?
This is a research study because the study doctors are interested in investigating whether treatment with citric acid and potassium citrate can reduce the risk of recurrent kidney stones in people who form calcium phosphate stones.

The following definitions may help you understand this study:
- Double-blind means neither you nor the researchers will know which drug you are receiving.
- Placebo-controlled means that some participants will get a placebo. A placebo looks like the investigational drug but it includes no active ingredients (for example, a sugar pill).
- Randomization means you will be placed by chance (like drawing straws) in one of the study groups. You will undergo each phase by the end of the study.
- Standard medical care means the regular care you would receive from your personal doctor if you choose not to participate in this research.
- Researchers means the study doctor and research personnel at the University of Texas Southwestern Medical Center at Dallas and its affiliated hospitals.

Why am I being asked to take part in this research study?
You are being asked to take part in this study because you form calcium phosphate kidney stones and you have hypocitraturia (too little citrate in your urine).

How many people will take part in this study?
About 50 participants will take part in this study at UT Southwestern Medical Center or Parkland Health & Hospital System.

What is involved in the study?
If you agree to be in this study, you will be asked to sign this consent form and will have the following tests and procedures. The procedures are being done solely for the purpose of this study.

Screening Procedures
To help decide if you qualify to be in this study, the researchers may ask you questions about your health, including medications you take and any surgical procedures you have had.

You may also have to fill out certain forms or have the following exams, tests or procedures:

- Physical exam;
- Social and medical history;
- Vital signs;
- Blood tests (about 2 teaspoons): Comprehensive metabolic panel (sodium, potassium, chloride, bicarbonate, glucose, BUN, creatinine, calcium, total protein, albumin, bilirubin, alkaline phosphatase, AST, ALT), magnesium, phosphorus and uric acid;
- 24-hour urine tests: total volume, pH, creatinine, sodium, potassium, calcium, magnesium, phosphorus, oxalate, uric acid, sulfate, citrate, chloride and ammonium, spot urinalysis, and physicochemical assays (concentration product ratio, crystal growth, formation product);
- Urine pregnancy test in women of child-bearing age;
- Demographic information (age, gender, ethnic origin);
- Personal information (name, date of birth, address, telephone number, emergency contact, and referring physician)

Existing fasting blood and 24-hour urine results will be extracted from your medical records, if available, from the previous 12 months. If you have not had certain tests performed within the past 12 months, you will be asked to do so for screening purposes. The amount of blood drawn will be about two teaspoons.

Group Assignment
If the researchers believe you can take part in this study, you will be assigned randomly (like drawing straws) to receive placebo, citric acid, or potassium citrate. You will participate in all three phases by the end of this study. The order in which you receive these will be decided by a biostatistician. Neither you nor the researchers will be allowed to choose which phase you are in. However, the sponsor will release the information about your assignment to the researchers if it is needed for your safety.

Study Medication/Intervention
If you decide to participate in this study you will take:

- 3 tablets of citric acid (10 milliequivalents/tablet) twice a day.
- 2 tablets of potassium citrate (10 milliequivalents/tablet) and one placebo tablet twice a day.
- 3 tablets of matching placebo twice a day.

Procedures and Evaluations during the Research

You will undergo an inpatient evaluation including two overnight stays at the Clinical and Translational Research Center (CTRC) during each of the three study phases. You will undergo the following procedures during each one week phase. Each phase will be followed by a one week washout period, in which you do not take any study medication.

Days 1-2:
- You will be instructed to adhere to a specific diet at home.

Days 3-5:
- You will be given frozen metabolic meals prepared by the Clinical & Translational Resource Center (CTRC) metabolic kitchen. These meals are to be eaten for five days before your inpatient evaluation at the CTRC. You must eat all of the prepared meals and must not eat anything in addition to what you are given.

Days 6-8:
- You will be admitted to the CTRC on the morning of day 6.
- You will continue to receive metabolic meals prepared by the CTRC metabolic kitchen.
- *Urine:* On day 6 and 7 you will collect your urine for 24 hours (22-hr urine and 2-hr fasting urine collections).
- *Blood*: Fasting blood will be obtained at the end of each urine collection on days 7 and 8.
- You will be discharge from the CTRC on the morning of day 8.

The tests performed in this study are designed for research, not for medical purposes. Even though the researchers are not looking at these tests to find or treat a medical problem, you will be told if they notice something unusual. You and your regular doctor can decide together whether to follow up with more tests or treatment. Because the tests being done in this study are not for medical purposes, the research results will not be sent to you or to your regular doctor.

Procedures for storing of extra or left over samples

Participant data will be recorded in a password-protected master enrollment database where each subject is given a unique numeral identifier. These numbers will be retained throughout the study and referenced in lieu of identifiable patient information. This procedure thereby de-identifies the data yet maintains a confidential and secure link for investigators. Access to the master database will be restricted solely to key personnel on an "as-needed" basis. The ability to alter data in the study databases or directly view all of it will be limited to the PI, biostatistician, and research coordinator.

How long can I expect to be in this study?

The duration of this study is 5 weeks. You can choose to stop participating for any reason at any time. However, if you decide to stop participating in the study, we encourage you to tell the researchers. You may be asked if you are willing to complete some study termination tests.

What are the risks of the study?

Study Procedure/Intervention

Because of your participation in this study, you are at risk for the following side effects. You should discuss these with the researchers and your regular health care provider.

The study drugs may cause some, all, or none of the side-effects listed below.

Citric Acid:

Common (frequency not defined)	Rare but Serious (frequency not defined)
• Diarrhea	• Hypocalcemia (low blood calcium)
• Nausea	• Metabolic Alkalosis
• Vomiting	

Potassium Citrate:

Common (frequency not defined)	Rare but Serious (frequency not defined)

- Diarrhea
- Abdominal pain
- Gastric mucosal erosion
- Nausea
- Vomiting
- Hyperkalemia (high blood potassium)
- Cardiac arrest

Loss of Confidentiality

Any time information is collected; there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

Risks to an Embryo, Fetus or Breast-fed Infant

Females: If you are part of this study while pregnant or breast-feeding an infant, it is possible that you may expose the unborn child or infant to risks. For that reason, pregnant and breast-feeding females cannot participate in the study. If you can become pregnant, a blood or urine pregnancy test will be done (using 1 teaspoon of blood drawn from a vein by needle-stick), and it must be negative before you participate in this study. If you take part in this study and you are sexually active, you and any person that you have sex with must use medically-acceptable birth control (contraceptives) during the study. Medically-acceptable birth control (contraceptives) includes:

1. Surgical sterilization (such as hysterectomy or "tubes tied"),
2. Approved hormonal contraceptives (such as birth control pills, Depo-Provera, Depo-Lupron, patch or ring),
3. Barrier methods (such as condom or diaphragm) used with a spermicide (a substance that kills sperm), or
4. An intrauterine device (IUD).

If you do become pregnant during this study, you must tell the researchers immediately.

Risks of Blood Drawing

Risks associated with drawing blood from your arm include minimal discomfort and/or bruising. Infection, excess bleeding, clotting, dizziness, and/or fainting also are possible, although unlikely. You will have 9 tablespoon (3 tablespoons per phase) of blood collected because you are in this research study.

Placebo

If you receive a placebo, you will not receive active medication for your health problem. If your problem becomes worse, your participation in the research will stop. If this happens, your study doctor can discuss alternative care with you.

Other Risks

There may possibly be other side effects that are unknown at this time. If you are concerned about other, unknown side effects, please discuss this with the researchers.

How will risks be minimized or prevented?

We will ask for your consent prior to your participation in the study. All efforts will be utilized to ensure subject privacy and all data will be held confidentially. Your study participation will be monitored for any unexpected side effects and the investigators will be alerted immediately in the case of any patient concerns. Participation in the study will be terminated if you request to withdraw.

What will my responsibilities be during the study?

While you are part of this study, the researchers will follow you closely to determine whether there are problems that need medical care. It is your responsibility to do the following:

- Ask questions about anything you do not understand.
- Keep your appointments.
- Follow the researchers' instructions.
- Let the researchers know if your telephone number or address changes.
- Store study medications a secure place at home away from anyone who is unable to read and understand labels, especially children.
- Tell the researchers before you take any new medication, even if it is prescribed by another doctor for a different medical problem or something purchased over the counter.
- Tell your regular doctor about your participation in this study.
- Report to the researchers any injury or illness while you are on study even if you do not think it is related.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
Yes. You will be told if any new information becomes available during the study that could cause you to change your mind about continuing to participate or that is important to your health or safety.

What should I do if I think I am having problems?
If you have unusual symptoms, pain, or any other problems while you are in the study, you should report them to the researchers right away. Telephone numbers where they can be reached are listed on the first page of this consent form.

If you have a sudden, serious problem, like difficulty breathing or severe pain, go to the nearest hospital emergency room, or call 911 (or the correct emergency telephone number in your area). Tell emergency personnel about any medications you are taking, including any medications you are taking for this study.

What are the possible benefits of this study?
If you agree to take part in this study, there will not be direct benefits to you. The researchers cannot guarantee that you will benefit from participation in this research.

We hope the information learned from this study will benefit others who form calcium phosphate kidney stones in the future. Information gained from this research could lead to better medical care for these individuals.

What options are available if I decide not to take part in this research study?
You do not have to participate in this research to receive care for your medical problem. Instead of being in this study, you have the following options:

- You may concentrate on further increasing your fluid intake
- You may further reduce your salt intake and moderate your protein intake

Will I be paid if I take part in this research study?
Yes. You will be paid $475 at the end of the study. If you stop taking part in this study or are withdrawn by the research team, you will receive payment for only the visits you have completed. For example, you will be paid $150 for completing phase I, $150 for completing phase II, and $150 for completing phase III, plus an additional $25 for completing the entire study.

There are no funds available to pay for parking expenses, transportation to and from the research center, lost time away from work and other activities, lost wages, or child care expenses.

How will I be paid?
You will be issued a UT Southwestern Greenphire ClinCard, which can be used as a credit or debit card. You will also receive instructions on how to use the card. In order to receive study payments, your name, address, date of birth and Social Security Number (SSN) will be collected from you by the research staff. All information will be stored in a secure fashion and will be deleted from the UT Southwestern Greenphire ClinCard system once the study has been completed.

Important Information about Study Payments

1. Your SSN is needed in order to process your payments. Should you decide not to provide your SSN, your study participation payment will be decreased at the current IRS tax rate. Study payments are considered taxable income and are reportable to the IRS.
2. An IRS Form 1099 will be sent to you in your total payments are $600 or more in a calendar year.
3. Your payment information will not be shared with any third parties and will be kept completely confidential.

This payment information will remain confidential unless you give your permission to share it with others, or if we are required by law to release it.

UT Southwestern, as a State agency, will not be able to make any payments to you for your participation in this research if the State Comptroller has issued a "hold" on all State payments to you. Such a "hold" could result from your failure to make child support payments or pay student loans, etc. If this happens, UT Southwestern will be able to pay you for your taking part in this research 1) after you have made the outstanding payments and 2) the State Comptroller has issued a release of the "hold".

Will my insurance provider or I be charged for the costs of any part of this research study?
No. Neither you, nor your insurance provider, will be charged for anything done only for this research study (i.e., the Screening Procedures or Experimental Procedures described above).

What will happen if I am harmed as a result of taking part in this study?
It is important that you report any illness or injury to the research team listed at the top of this form immediately. Compensation for an injury resulting from your participation in this research is not available from the University of Texas Southwestern Medical Center at Dallas or Parkland Health and Hospital System.

You retain your legal rights during your participation in this research

Can I stop taking part in this research study?
Yes. If you decide to participate and later change your mind, you are free to stop taking part in the research study at any time.

If you decide to stop taking part in this research study, it will not affect your relationship with the UT Southwestern staff or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

If you are a medical student, fellow, faculty, or staff at the Medical Center, your status will not be affected in any way.

Your doctor is a research investigator in this study. S/he is interested in both your medical care and the conduct of this research study. At any time, you may discuss your care with another doctor who is not part of this research study. You do not have to take part in any research study offered by your doctor.

If I agree to take part in this research study, can I be removed from the study without my consent?

Yes. The researchers may decide to take you off this study if:

- The researchers believe that participation in the research is no longer safe for you.
- The sponsor or the FDA stops the research for the safety of the participants.
- The sponsor cancels the research.
- You are unable to keep appointments or to follow the researcher's instructions.

Will my information be kept confidential?

Medical information collected during this study and the results of any test or procedure done may be included in your medical record and this information may be available to health care providers and authorized persons including your insurance company. Information about you that is collected for this research study will remain confidential unless you give your permission to share it with others, or if we are required by law to release it. You should know that certain organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- Representatives of government agencies, like the U.S. Food and Drug Administration (FDA), involved in keeping research safe for people; and
- The UT Southwestern Institutional Review Board.

In addition to this consent form, you will be asked to sign an "Authorization for Use and Disclosure of Protected Health Information." This authorization will give more details about how your information will be used for this research study, and who may see and/or get copies of your information.

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by the U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Are there procedures I should follow after stopping participation in this research?

Yes. If you, the researchers, or the sponsor stops your participation in the research, you may be asked to do the following:

- Let the researchers know immediately that you wish to withdraw from the research.
- Return to the research center for tests that may be needed for your safety.
- Return any unused study materials, including empty containers.
- Discuss your future medical care, if any, with the researchers and/or your personal doctor.

Whom do I call if I have questions or problems?

For questions about the study, contact Dr. Naim Maalouf at 214-648-2954 during regular business hours and at 214-648-6888 after hours and on weekends and holidays.

For questions about your rights as a research participant, contact the UT Southwestern Institutional Review Board (IRB) Office at 214-648-3060.

SIGNATURES:

YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.

Your signature below certifies the following:

- You have read (or been read) the information provided above.
- You have received answers to all of your questions and have been told who to call if you have any more questions.
- You have freely decided to participate in this research.
- You understand that you are not giving up any of your legal rights.
- You understand that a copy of this signed consent document, information about this study and the results of any test or procedure done may be included in your medical record and this information may be available to health care providers and authorized persons including your insurance company.

Signature of Participant (18 yrs or older)	Printed Name of Participant (18 yrs or older)	Date	Time	AM/PM

NAME OF PERSON OBTAINING CONSENT

Signature	Printed Name	Date	Time	AM/PM